Remarks

Specification:

Applicants have amended the specification as suggested in the Office Action. Replacement pages have been submitted incorporating the changes.

Rejection of claims under 35 U.S.C. 112:

Claims 1-3 and 3-39 were rejected under §112 as not being enabling for the methods claimed.

Applicants have amended independent claims 1 and 39 to clarify the method of delivery and the target cells. On page 5, paragraph 2, "The specification does not teach targeting any parenchymal cell other than skeletal muscle cells." The claims have thus been amended to specify delivery of polynucleotides to skeletal muscle cells as well as to clearly indicate the blood vessel into which the polynucleotide is injected and the skeletal muscle cells to which the polynucleotide is delivered. The amended claims further clarify the method of impeding blood flow as well as the location of the injection and the target cells relative to the placement of the blood vessel occlusion.

Teachings and support for delivery to "skeletal muscle cells" can be found on page 3 lines 5-6, page 10 line 19-21, example 1 starting on page 23, example 3 starting on page 25, example 7 on page 30, and examples 8 and 9 on page 31 of the specification. Teachings and support for "inserting an injector into a limb blood vessel of the mammal" can be found on page 2 lines 28-29, page 3 lines 2-3 and 14, page 4 line 32, page 5 line 5-7, page 10 line 20, page 16 lines 10-16, page 17 lines 8-31, page 23 lines 16-23, page 25 line 32 bridging to page 26 line 1, and page 31 lines 9-12 of the specification. Teachings and support for "limb blood vessel of the mammal" can be found on page 5 lines 22-24, page 10 lines 19-20, example 1 starting on page 23, example 3 starting on page 25, examples 6 and 7 an page 30, and examples 8 and 9 on page 31 of the specification. Teachings and support for "applying device external to mammalian skin for occluding blood vessels in the limb" can be found on page 3 lines 8-11, page 5 lines 7-8, and page 5 lines 13-24 and in the examples of the specification. Teaching and support for "injecting a solution containing the polynucleotides into the lumen of the vessel distal to the occlusion" can be found on page 16 lines 10-16, page 23, lines 22-25, example 3 starting on page 25, example 7 on page 30, and example 8 on page 31 of the specification.

The applicants respectfully disagree with the examiner concerning the terms anterior, posterior and superficial muscle cells. These are terms of art that specify the location of the muscle relative to its position in the mammal itself, and not to the position of the mammal relative to a viewer. However, the applicants have canceled claims 10, 15, 23, and 27 concerning deep or interior muscle cells and have amended claims 11 and 12 to remove the ambiguous abbreviations. Spf. and prof. are abbreviations of the terms superficialis and profundus, respectively. These abbreviations appear in the table on page 26 of the specification. The unabbreviated terms were substituted for the abbreviations in claims 11 and 12 as requested by the Examiner. Because amended claims 11 and 12 now contain unabbreviated terms for the previously abbreviated terms, no new matter was introduced.

The term anterior was added to claim 12 because claim 10, from which claim 12 originally depended was cancelled. Claim 12 was amended to depend from claim 8. Claim 10 originally

depended from claim 8. Therefore no new matter was introduced by the addition of the term anterior to claim 12.

The term posterior was added to claim 17 because claim 15, from which claim 17 originally depended was cancelled. Claim 17 was amended to depend from claim 13. Claim 15 originally depended from claim 13. Therefore no new matter was introduced by the addition of the term posterior to claim 17.

The term posterior muscle was added to claim 25 because claim 23, from which claim 25 originally depended was cancelled. Claim 25 was amended to depend from claim 21. Claim 23 originally depended from claim 21. Therefore no new matter was introduced by the addition of the term posterior muscle to claim 25.

The term leg muscle cell was substituted for the term interior muscle cell in claim 30 because claim 27, from which claim 30 originally depended was cancelled. Claim 30 was amended to depend from claim 6. Claim 27 originally depended from claim 6. Therefore no new matter was introduced by the addition of the term leg muscle cell to claim 30.

Claim 33 has been amended to substitute the term occluding blood vessels for externally applying pressure to properly depend from amended claim 1. Teachings and support for occluding blood vessels can be found on page 3 lines 8-11, page 5 lines 7-8, and page 5 lines 13-24 and in the examples of the specification.

Applicants have either cancelled or amended the claims to obviate the rejections. Applicants respectfully request that the §112 rejections be removed.

Rejection of claims under 35 U.S.C. 102:

Claims 1-32 and 37-39 were rejected under §102(b) as being anticipated by Milas, Sferra and Nabel. Milas and Sferra teach adenoviral delivery to hepatocytes and intestinal cells, respectively. Nabel teaches delivery exclusively to vascular cells, immune cells and vessel smooth muscle cells. As noted above, Applicants have amended the claims to specify delivery to limb skeletal muscle cells.

Claims 1-3, 8-10, 13-15, 32, and 38-39 were rejected under §102(e) as being anticipated by Wolff. Wolff taught injection of polynucleotide into heart interstitium, which the examiner considers a vessel that contains blood. The amended claims more clearly specify injection of the polynucleotide into a limb blood vessel and delivery to limb skeletal muscle cells.

Applicants believe that the amended claims obviate the rejections since the prior art does not teach the use of a noninvasive external device to aid in the delivery of polynucleotides to limb skeletal muscle cells. In fact, as the examiner notes on page 5, both Milas and Ye, failed to observe delivery of polynucleotide to muscle cells after injection of adenovirus into the femoral artery or the retroorbital venous plexus (Milas et al 1997, page 2201 column 2, line 16-18; Ye et al 2000, page 623, column 2, lines 16-18). Rather, both researchers observed delivery to liver. In contrast, applicants have clearly shown delivery of polynucleotides to skeletal muscle using the claimed processes, see examples 1 & 3 (primate), and examples 5, 7, 8, 9 and 10 (rat).

The Examiner's objections and rejections are now believed to be overcome by this response to the Office Action. In view of Applicants' amendment and arguments, it is submitted that claims 1-4, 6-9, 11-14, 16-22, 24-26, 28-31, 33-36 and 39-40 should be allowable and Applicants respectfully requests an early notice to such effect.

Respectfully submitted,

Mark K. Johnson Reg. No. 35,909
Mirus
505 South Rosa Road
Madison, WI 53719
608.238.4400

I hereby certify that this correspondence is being facsimile transmitted to the USPTO 703.308.4242 addressed to: Commissioner for Patents, Alexandria, VA, 22313 on: August 11, 2003.

Kirk Ekena

OFFICIAL